[CONTRIBUTION FROM THE PATHOLOGICAL DIVISION, BUREAU OF ANIMAL INDUSTRY]

Lupine Studies. VI. The Alkaloids of Lupinus Corymbosus, Heller. Part 1

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Lupinus corymbosus is one of the Pacific coast species of lupine and is found growing from Nevada to Eastern Oregon. It is a shrubby perennial often cultivated for its handsome flowers and foliage. In some places it grows very thickly and may become a menace to livestock. It has not previously been examined chemically. Material of this species was collected in 1930 and from it a mixture of alkaloids was obtained which has yielded a new lupine alkaloid.

The new base has the composition $C_{15}H_{20}N_2O$, and is isomeric with anagyrine recently reported by Ing[1] and with thermopsine isolated by Oryekhov, Norkina and Gurevich.[2] It differs in chemical and physical properties from these bases, however, and from the hitherto known lupine alkaloids as well. It contains four hydrogen atoms per molecule less than lupanine and this indicated unsaturation is confirmed by its behavior toward neutral potassium permanganate solution which it rapidly reduces and toward gold chloride solutions from which it slowly precipitates metallic gold. The oxygen atom is indifferent as in the case of lupanine. Attempts to acylate the base with acetic anhydride or benzoyl chloride were unsuccessful. It gives a red color with ferric chloride in water solution. It decomposes hydriodic acid with formation of red periodides. It responds to the modified Grant's test[3] for sparteine but the color developed is less blue-red than with sparteine. Hydrogenation experiments indicate that the substance takes up hydrogen with some difficulty. The products of the reaction have not yet been identified. The new base has been named hexalupine.

Note on the Nomenclature of the Lupine Alkaloids.—The naming of new lupine alkaloids presents certain problems that cannot be solved by following the somewhat loose rules now in vogue for naming alkaloids. The terminological possibilities of the generic name have already been exhausted by the names, lupinine, lupanine, lupinidine, lupanidine, isolupinine and allolupinine. Recourse to the specific names involves difficulties, for in the genus *Lupinus* many specific names are unsuited for coining new names, either because of lack of euphony or because of possible confusion with established names of compounds.[4] We have gathered evidence in this Laboratory of some twenty new lupine alkaloids, the chemical examinations of which are in several instances well advanced. We now propose to designate these alkaloids by a numerical system affixing the Greek numeral prefixes to the generic word lupine, the ending of which happily conforms to usage in naming bases. Thus we shall have monolupine from *L. caudatus*, dilupine and trilupine from *L. barbiger*, tetralupine and pentalupine from *L. palmeri*, instead of possibly caudatine, barbigine and barbiginine, palmerine and palmeridine. This sytem will immediately classify the alkaloids as to source and can be adapted to indicate chemical relationships.

Experimental

Collection of Plant Material.—The plant material used in this investigation was collected on August 29 and September 2, 1930, in the neighborhood of Hager Station, two miles south of Klamath Falls, Oregon. The plant was in full bloom. A few specimens had formed pods that contained ripe seeds. All the above-ground parts were included in the collection. The material was spread out and allowed to dry in the sun. It was then bagged and shipped to the laboratory in Washington, D. C., where it was ground to a coarse powder and stored for use.[5] The botanical identification was made by Mr. Ivar Tidestrom of the Bureau of Plant Industry and a specimen of the plant has been deposited in the U. S. National Herbarium, no. 1,184,339.

Moisture.—Samples of the ground air-dried plant yielded 7.66% of moisture at 125°.

Extraction of the Alkaloids.—24.695 kg. of air-dried plant was extracted with alcohol as long as the percolate gave a positive test with Mayer's reagent. The solvent was distilled off and the residue was extracted repeatedly with boiling water. The water solutions were siphoned off, let cool, filtered and concentrated to 8 liters. The water solution was allowed to stand at room temperature for three months, when a large quantity of non-basic crystalline material was deposited. This was collected and recrystallized from boiling water. It gave some tests for glucosides. It was preserved for further investigation.

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(1) *J. Chem. Soc.*, 504–510 (1933).

(2) *Ber.*, **66**, 621–625 (1933).

(3) *Am. J. Pharm.*, **97**, 38 (1925).

(4) For example, such specific names as malacophyllus, flavoculatus, shockleyi, odoratus, argenteus, sericeus, arizonicus, nevadensis, arboreus or sulphureus.

(5) The writer wishes to express his appreciation of the assistance furnished him by E. R. Kalmbach and Dr. J. E. Schillinger, of the Bureau of Biological Survey, in making the collections.

The water solution was now treated with excess of a hot solution of basic lead acetate. The voluminous yellow precipitate was filtered off, washed thoroughly, and the washings were added to the first filtrate. This was freed from lead with sulfuric acid, filtered, concd. to 3 liters, made alkaline with sodium hydroxide and shaken out with chloroform in successive portions.

The chloroform was distilled from the extracted alkaloids, which assumed the form of a red-brown sirup. After a few days' standing this sirup deposited a mass of needles mixed with tarry matter. The fluid portions were poured off, mixed with methanol and the remaining chloroform was distilled off as the azeotropic mixture with methanol. The residue deposited more needles which were collected and added to the first portion. The crystalline material weighed 122.5 g. and the mother liquor, 465.5 g., a total of 588 g. or 2.60% of the moisture-free plant. Examination of the mother liquor is in progress.

Isolation of Hexalupine

The crystalline fraction was warmed with successive portions of ethyl acetate which dissolved the crystals leaving the tarry impurities undissolved. On cooling the ethyl acetate solution in an ice box there was deposited a mass of clumped yellowish needles that melted at 187–191°. These were recrystallized twice from ethyl acetate without affecting the melting point. Then they were recrystallized from alcohol a number of times until the melting point was constant at 197–198°.

Anal. Calcd. for $C_{15}H_{20}N_2O \cdot {}^1/_3H_2O$: C, 71.97; H, 8.32; N, 11.20; H_2O, 2.40%. Found: C, 72.18, 72.02; H, 8.47, 8.42; N, 11.11, 11.07; H_2O, 2.38, 2.38. In alcohol, $[\alpha]^{29}_{D}$ 126.1°, c = 4.795 g., l = 1, a = 6.044°.

Hexalupine crystallizes easily from alcohol or dilute alcohol in stubby prisms soluble in ether, chloroform and acetone, less soluble in petroleum ether. It is less soluble in water than is usual with lupine alkaloids and is not more soluble in cold than in hot water, differing from lupinine, lupanine, and sparteine. It instantly reduces a cold solution of potassium permanganate and slowly reduces an acid solution of gold chloride. Its solutions are strongly alkaline to litmus.

Hexalupine Dihydrochloride.—Five grams of hexalupine was dissolved in 25 cc. of boiling acetone and to the cooled solution 7 cc. of concd. hydrochloric acid was added. The mixture boiled and a gummy mass was thrown out. Enough alcohol (10 cc.) was added to bring the precipitate back into solution. As the solution cooled a quantity of small white plates was deposited. These were collected on a suction filter, washed with 50% acetone–alcohol, recrystallized from the same solvent, and dried for several days in a desiccator over calcium chloride; m. p. 116° sharp on rapid heating. Slow heating gives a higher melting point, due to formation of monohydrochloride.

The substance proved to be a dihydrochloride. On heating to 125° to remove moisture it gave off half of its hydrochloric acid and enough moisture to correspond to three molecules of water. A test for acetone of crystallization was negative.

Anal. Calcd. for $C_{15}H_{20}N_2O \cdot 2HCl \cdot 3H_2O$: Cl, 19.14; $1HCl \cdot 3H_2O$, 24.40. Found: Cl, 18.94, 18.81; "moisture," 24.62, 24.60. In water $[\alpha]^{29}_{D}$ 106.5°, c = 3.192 g., l = 1, a = 3.399°. The substance is soluble in water but could not be recrystallized from that solvent.

Hexalupine Monohydrochloride.—The residue obtained by heating the dihydrochloride to constant weight at 125° proved to be the monohydrochloride. It has not as yet been recrystallized. This substance is extremely hygroscopic and it was difficult to get accurate data concerning it. It softens at 122° and melts at 136–138°. A sample prepared by very slowly heating the dihydrochloride in a melting-point tube melted at 304–305°, which is considered the true figure.

Anal. Calcd. for $C_{15}H_{20}N_2O \cdot HCl$: Cl, 12.65. Found: Cl, 12.95, 12.45. Calculated to the dihydrochloride these figures become: calcd. 9.57; found, 9.76, 9.40 or half that found for the dihydrochloride.

Hexalupine Gold Chloride.—One gram of the alkaloid was dissolved in 10 cc. of water and few drops of hydrochloric acid. To this was added an excess of gold chloride solution. The heavy curdy yellow precipitate was recrystallized from hot water containing a little hydrochloric acid; golden needles, m. p. 204° dec. The mother liquors on standing deposited a film of metallic gold.

Anal. Calcd. for $C_{15}H_{20}N_2O \cdot 1.5HAuCl_4.2 \cdot 5H_2O$: Au, 36.95; H_2O, 5.61. Found: Au, 37.08; H_2O, 5.94.

Hexalupine Picrate.—To 1 g. of hexalupine dissolved in 10 cc. of alcohol was added an alcoholic solution of picric acid. A gummy yellow ppt. fell which was recrystallized from hot 70% alcohol as lemon yellow needles darkening at 210° and melting at 245–246°.

Summary

A new alkaloid, hexalupine, $C_{15}H_{20}N_2O$, has been isolated from *Lupinus corymbosus*, Heller. A description of the alkaloid and some of its salts is given. A new system for naming lupine alkaloids is proposed.

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RECEIVED AUGUST 21, 1933